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(74) Common Representative: MERCK & CO., INC.: 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US).

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(71) Applicant (for all designated States except US): MERCK & CO., INC. [US/US]: 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US).

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(72) Inventors; and

(75) Inventors/Applicants (for US only): SHIVER, John, W. [US/US]: 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US). LIANG, Xiaoping [CA/US]: 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US). FU, Tong-Ming [US/US]: 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US).

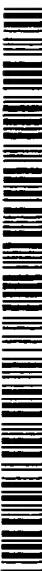
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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.



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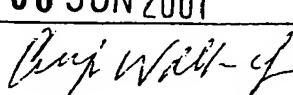
(54) Title: POLYNUCLEOTIDE VACCINES EXPRESSING CODON OPTIMIZED HIV-1 NEF AND MODIFIED HIV-1 NEF

(57) Abstract: Pharmaceutical compositions which comprise HIV Nef DNA vaccines are disclosed, along with the production and use of these DNA vaccines. The nef-based DNA vaccines of the invention are administered directly introduced into living vertebrate tissue, preferably humans, and express the HIV Nef protein or biologically relevant portions thereof, inducing a cellular immune response which specifically recognizes human immunodeficiency virus-1 (HIV-1). The DNA molecules which comprise the open reading frame of these DNA vaccines are synthetic DNA molecules encoding codon optimized HIV-1 Nef and derivatives of optimized HIV-1 Nef, including nef modifications comprising amino terminal leader peptides, removal of the amino terminal myristylation site, and/or modification of the Nef dileucine motif. These modifications may effect wild type characteristics of Nef, such as myristylation and down regulation of host CD4.

INTERNATIONAL SEARCH REPORT

International application No.

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| A. CLASSIFICATION OF SUBJECT MATTER | | |
| IPC(7) : C07H 21/04; C12N 15/00; A61K 39/00 US CL : 536/23.4; 435/320.1; 424/184.1 According to International Patent Classification (IPC) or to both national classification and IPC | | |
| B. FIELDS SEARCHED | | |
| Minimum documentation searched (classification system followed by classification symbols) U.S. : | | |
| Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched | | |
| Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) Medline, caplus, biosis, embase, scisearch, wpids. | | |
| C. DOCUMENTS CONSIDERED TO BE RELEVANT | | |
| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| X | TOBERY, T. et al. Cutting Edge: Induction of Enhanced CTL-Dependent Protective Immunity in vivo by N-End Rule Targeting of a Model tumor Antigen. 15 Jan 1999, 162 (2) 639-642. (see abstract) | 1,2,6,7,20-22, 26-28 |
| X | GIRARD, M. New prospect for the development of a vaccine against human immunodeficiency virus type 1. An overview. Comptes Rendus de L Academie Des sciences. Serie III, Sciences de la vie, November 1999, 322 (11) 959-66. | 1,2,6,7,20-22, 26-28 |
| Y | US 5,851,813 A (DESROSIERS) 22 December 1998, see abstract | 1,2,6,7,20-22, 26-28 |
| <input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex. | | |
| * Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed | | |
| "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family | | |
| Date of the actual completion of the international search | Date of mailing of the international search report | |
| May 4, 2001 | 06 JUN 2001 | |
| Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230 | Authorized officer Eleanor Sorbello  Telephone No. 703-308-0196 | |

INTERNATIONAL SEARCH REPORT

International application No.

PC S00/34162

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claim Nos.: because they relate to subject matter not required to be searched by this Authority, namely:

2. Claim Nos.: 3-5,8-19,23-25 and 29 because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
Please See Continuation Sheet

3. Claim Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

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Continuation of Box I Reason2: Claims 3-5, 8-19, 23-25 and 29 were not searched as the application did not comply with sequence rules. The CRF was found to be defective. A CRF Error Report was faxed to Mark Hand on March 3, 2001. However, corrected diskette has not been submitted.